In the specification:

Please replace the current Sequence Listing with the substitute Sequence Listing submitted herewith.

Please amend the paragraph beginning at page **5**, line **1** as follows:

Accordingly, the present invention provides novel methods for the treatment of insulin dependent (type-I) diabetes in a prediabetic. In particular, the present invention provides a method for the prevention of insulin dependent diabetes comprising the step of administering to a prediabetic individual a VLA4 blocking agent, e. g., a soluble VCAM-IgG fusion protein or an 5 anti-VLA-4 antibody, such as antibody HP1/2 or a humanized anti-VLA-4 antibody derived from HP1/2. Also contemplated is the use of analogous antibodies, antibody fragments, soluble proteins and small molecules, e. g., those that mimic the action of anti-VLA-4 antibodies in the treatment of diabetes. In addition, the present invention provides a method for the treatment of diabetes by administering to a mammal, including a human with a susceptibility to diabetes, a 10 VLA-4 blocking agent, e. g., a soluble VCAM-IgG fusion protein, or an antibody capable of binding to the α4 subunit of VLA-4 in an amount effective to provide inhibition of the onset of diabetes. Also contemplated is the use of recombinant and chimeric antibodies, fragments of such antibodies, polypeptides or small molecules capable of binding α4/NLA-4 or a VLA-4 ligand. Also contemplated are soluble forms of the natural binding proteins for VLA4, including soluble VCAM-1, VCAM-1 peptides or VCAM-1 fusion proteins as well as fibronectin, fibronectin having an alternatively spliced non-type III connecting segment and fibronectin peptides containing the amino acid sequence EILDV (SEQ ID NO:19) or a similar conservatively substituted amino acid sequence. These agents block VLA-4, e.g., by competing with the cellsurface binding protein for VLA-4 or by otherwise altering, inhibiting or blocking VLA-4 function.

Please amend the paragraph beginning at page **8**, line **11** as follows:

As discussed herein, the blocking agents used in methods of the invention are not limited to antibodies or antibody derivatives, but may be other molecules, e.g., soluble forms of other proteins which bind VLA-4, e.g., the natural binding proteins for VLA-4. These binding agents

include soluble VCA M-1 or VCA M-1 peptides, VCAM -1 fusion proteins, bifunctional VCAM l/Ig fusion proteins, fibronectin, fibronectin having an alternatively spliced non-type III connecting segment, and fibronectin peptides containing the amino acid sequence EILDV (SEQ ID NO:19) or a similar conservatively substituted a mino acid sequence. These binding agents can act by competing with the cell-surface binding protein for VLA-4 or by otherwise altering VLA-4 function. For example, a soluble form of VCAM-1 (see, e.g., Osbom et al. 1989 [58]) or a fragment thereof may be administered to bind to VLA-4, and preferably compete for a VLA-4 binding site, thereby leading to effects similar to the ad ministration of anti-VLA-4 antibodies. Soluble VCAM-1 fusion proteins can be used in the methods described herein. For example, VCAM-l, or a fragment thereof which is capable of binding to VLA-4 antigen on the surface of VLA-4 bearing cells, e.g., a fragment containing the two N-ter minal domains of VCA-1, can be fused to a second peptide, e.g., a peptide which increases the solubility or *the in vivo* life time of the VCA M-1 moiety. The second peptide can be a fragment of a soluble peptide, preferably a human peptide, more preferably a plasma protein, or a member of the immunoglobulin super fa mily. In particularly preferred embodiments the second peptide is IgG or a portion or fragment thereof, e.g., the human IgGl heavy chain constant region. A particularly preferred fusion protein is the VCAM 2D-IgG fusion.

Please amend the paragraph beginning at page **9**, line **26** as follows:

In another aspect the invention features a chimeric molecule which includes: (1) a VLA-4 targeting moiety, e.g., a VCAM-1 moiety capable of binding to VLA-4 antigen on the surface of VLA-4 bearing cells; (2)optionally, a second peptide, e.g., one which increases solubility or *in vivo* life time of the VLA-4 targeting moiety, e.g., a member of the immunoglobulin super family or fragment or portion thereof, e.g., a portion or a fragment of IgG, e.g., the human IgGl heavy chain constant region, e.g., C_H2 and C_H3 hinge regions; and (3) a toxin moiety. The VLA-4 targeting moiety can be any naturally occurring VLA-4 ligand or fragment thereof, e.g., a VCAM-1 peptide, fibronectin, fibronectin having an alternatively spliced non-type III connecting segment, and fibronectin peptides containing the amino acid sequence EILDV (SEQ ID NO:19) or a similar conservatively substituted amino acid sequence. A preferred targeting moiety is a soluble VCAM-1 fragment, e.g., the N-terminal domains 1 and 2 of the VCAM-1 molecule. The

toxin moiety can be any agent which kills or inactivates a cell when the toxin is targeted to the cell by the VLA-4 targeting moiety. Toxin moieties include: cytotoxic peptide moieties, e.g., Diphteria toxin A, *Pseudomonas* Exotoxin, Ricin A, Abrin A, *Schigella* toxin, or Gelonin; radionucleotides; and chemotherapeutic agent.

Please amend the paragraph beginning at page **12**, line **33** as follows:

Alternatively, as discussed above the binding agents used in the method according to invention may not be antibodies or antibody derivatives, but rather may be soluble forms of the natural binding proteins for VLA-4. These binding agents include soluble VCAM-1, VCAM-1 peptides, or VCAM-1 fusion proteins as well as fibronectin, fibronectin having an alternatively spliced non; type III connecting segment and flbronectin peptides containing the amino acid sequence EILDV (SEQ ID NO:19) or a similar conservatively substituted amino acid sequence. These binding agents can act by competing with the cell-surface binding protein for VLA-4.